AMENDMENTS TO THE SPECIFICATION

On page 14, line 23 to page 15 line 22, please:

replace "Lipitor"	with	-- LIPITOR® --,
replace "Baycol"	with	-- BAYCOL® --,
replace "Lascol"	with	-- LASCOL® --,
replace "Mevacor"	with	-- MEVACOR® --,
replace "Pravachol"	with	-- PREVACHOL® --,
replace "Zocor"	with	-- ZOCOR® --,
replace "Crestor"	with	-- CRESTOR® --,
replace "Peg-Intron"	with	-- PEG-INTRON® --,
after "PEGASYS"	insert	-- ® --,
replace "viraferon"	with	-- VIRAGERON® --,
replace "Zetia"	with	-- ZETIA® --,
replace "Sporonox"	with	-- SPORONOX® --,
replace "Ceplene"	with	-- CEPLENE® --,
replace "Maxamine"	with	-- MAXAMINE® --,
replace "Hepsera"	with	-- HEPSERA® --,
replace "Symmetrel"	with	-- SYMMETREL® --,
replace "Rebetron"	with	-- REBETRON® --,
replace "Rebetol"	with	-- REBETOL® --,
replace "Zeffix"	with	-- ZEFFIX® --,
after "EPIVIR"	insert	-- ® --,
after "3TC"	insert	-- ® --,
after "RETROVIR"	insert	-- ® --,
after "AZT"	insert	-- ® --,
replace "Ursodiol"	with	-- URSODIOL® --,
replace "Chenix"	with	-- CHENIX® --,
replace "Maxamime"	with	-- MAXAMINE® --,
replace "CellCept"	with	-- CELLCEPT® --,
replace "Imuran"	with	-- IMURAN® --,
replace "Deltasone"	with	-- DELTASONE® --,
replace "Orasone"	with	-- ORASONE® --,
replace "Neoral"	with	-- NEORAL® --,
replace "Sandimmune"	with	-- SANDIMMUNE® --,

replace	"Orthoclone OKT3"	with	-- ORTHOCLONE OKT3® --,
replace	"Prograf"	with	-- PROGRAF® --,
after	"FK506"	insert	-- ® --,
replace	"Rapamune"	with	-- RAPAMUNE® --,
replace	"OKT3 (Orthoclone) "	with	-- ORTHOCLONE OKT3® --; and,
replace	"Leucovorin"	with	-- LEUCOVORIN® --.

On page 43, lines 14, prior to the word "complexes", please insert -- to --.

Replacement sheets to the specification are attached which indicate the changes made. The sheets do not include new matter.

The genetic attachment of a T7 ligand to a recombinant therapeutic protein represents a method to attach the T7 ligand to a protein or peptide, i.e., the ligand can be produced as a fusion or chimeric protein. The T7 ligand may also be incorporated into viruses, such as adenovirus or retroviruses. The coiled-coil structure of the p17 protein rod domain, including the T7 ligand, may be incorporated into the triple-helix structure present in coat proteins of some viruses.

The T7 phage p17 hepatocyte targeting ligand can also be attached to a cargo compound via a spacer molecule such a PEG or chemically similar molecule. The PEG may shield the rod domain from nonproductive interactions with the cargo. Presenting the targeting ligand at the end of a PEG spacer may increase its accessibility to cell surface receptors. Other spacers or linkers include, but are not limited to, polysaccharides, dextrans, polymers, proteins, and acyl groups.

Other coupling methods are also possible provided that the coupling does not interfere with the targeting function of the p17 hepatocyte targeting function. Many cross-linking reagents are known in the art and available to link the ligand to a target compound.

A ligand is a compound that enhances binding to a cell in a selective manner. A ligand may increase binding of a compound to the cell surface and/or its association with an intracellular compartment. A ligand can be, but is not limited to: a protein, peptide, lipid, steroid, sugar, carbohydrate, or synthetic compound. The ligand may bind a target within the cell membrane, on the cell membrane or near a cell. Binding of a ligand to a receptor may initiate endocytosis. A ligand can modify a compound and can direct it to a cell type or location (such as tissue) either in culture or in a whole organism.

The general scheme for a liver targeted delivery system comprises the diagram shown in FIG. 2, wherein the system minimally consists of the T7 ligand and the cargo. The T7 ligand may be linked to the cargo by one or more additional elements such as is shown in the diagram. The attachment chemistry and linker may further include a variety of functional groups.

Functional group. Functional groups include cell targeting signals, nuclear localization signals, compounds that enhance release of contents from endosomes or other intracellular

vesicles (releasing signals), reactive groups, and other compounds that alter the behavior or interactions of the compound or complex to which they are attached.

Another functional group comprises compounds, such as polyethylene glycol, that decrease interactions between molecules and themselves and with other molecules. Such groups are useful in limiting interactions such as between serum factors and the molecule or complex to be delivered.

A linkage is an attachment that provides a covalent bond or spacer between two other groups (chemical moieties). The linkage may be electronically neutral, or may bear a positive or negative charge. The chemical moieties can be hydrophilic or hydrophobic. Preferred spacer groups include, but are not limited to C1-C12 alkyl, C1-C12 alkenyl, C1-C12 alkynyl, C6-C18 aralkyl, C6-C18 aralkenyl, C6-C18 aralkynyl, ester, ether, ketone, alcohol, polyol, amide, amine, polyglycol, polyether, polyamine, thiol, thio ether, thioester, phosphorous containing, and heterocyclic. The linkage may or may not contain one or more labile bonds. A spacer group can provide a means to increase the distance between the ligand and the cargo, shield the ligand from the cargo, provide attachment for multiple cargo compounds or multiple ligands, or provide better presentation or orientation of the ligand. An example of a spacer is a poly(ethyleneglycol), PEG, or similar molecule. The PEG would shield the rod domain from interaction with the cargo. Presenting the targeting ligand at the end of a PEG spacer may increase its accessibility to cell surface receptors.

Cargo may be selected from the list comprising: HMG CoA reductase inhibitors, [statins, statin class drugs, atorvastatin (~~Lipitor~~ LIPITOR®), cerivastatin (~~Baycol~~ BAYCOL®), fluvastatin (~~Lascol~~ LASCOL®), lovastatin (~~Mevacor~~ MEVACOR®), pravastatin (~~Pravachol~~ PREVACHOL®), simvastatin (~~Zocor~~ ZOCOR®), second generation statins, rosuvastatin (~~Crestor~~ CRESTOR®, ZD 4522)], interferons [interferon class drugs, modified interferons, pegylated interferon, pegylated interferon alfa-2b, ~~Peg-Intron~~ PEG-INTRON®, PEGASYS®, ~~viraferon~~ VIRAGERON®], cholesterol absorption inhibitors [~~Zetia~~ ZETIA®, ezetimibe, plant stanols], bile acid absorption inhibitors, bile acid sequestrants, anti-fungal drugs [Cytochrome P450 inhibitors, itraconazole (~~Sporonox~~ SPORONOX®), erythromycin], triglyceride lowering drugs [fibrates, fibric acid derivatives, gemfibrozil, bezafibrate], antiviral drugs [anti-hepatitis drugs, hepatitis therapeutics, histamine dihydrochloride, ~~Ceplene~~ CEPLENE® (~~Maxamine~~ MAXAMINE®), ~~Hepsera~~ HEPSERA®, adefovir dipivoxil 5-iodo-2'-deoxyuridine, Amantadine, ~~Symmetrel~~ SYMMETREL®], nucleotide/nucleoside analogs [nucleosides, Ribavarin, ~~Rebetron~~ REBETRON®, ~~Rebetol~~ REBETOL®, Lamivudine (~~Zeffix~~ ZEFFIX®, EPIVIR®, 3TC®), zidovudine (RETROVIR®, azidothymidine, AZT®, or ZDV)], anticholelithics/gallstone

methylmaleic anhydride per polymer primary amine in 10mM HEPES, 500 mM diisopropylethylamine at pH 8.0 or higher. This polymer was purified using a G-25 spin column to remove unreacted 2-propionic-3-methylmaleic anhydride. This modification converted that polycation to a pH-labile polyanion.

Attachment of T7 ligand to the polymer: Streptavidin (20mg, 10mg/mL) was brought up in 75 mM Sodium Phosphate, 75 mM NaCl, 5mM EDTA, pH 7.2. To this solution was added 10-15 mole eq. of LC-SPDP (100 mg/mL in DMF, Pierce). The solution was gently shaken for 1 h at RT. The SPDP modified streptavidin was then purified using a G-25 column. It was determined that each streptavidin had 8-12 PDP groups attach (Pyridine-2-Thione Assay). To the PDP-modified streptavidin was added 3 mol eq of Cys-PEG_{11}-T7 ligand (MC920) Coupling of the T7 ligand to the streptavidin was allowed to continue for 24 h at 4°C. This conjugate was purified on G-25 column, freeze dried and brought up at 3.0 mg/mL in 25 mM MES, 125 mM NaCl, pH 6.0. These polymers may then be used form to complexes with polynucleotide to facilitate delivery of the polynucleotide to hepatocytes.

The foregoing is considered as illustrative only of the principles of the invention. Furthermore, since numerous modifications and changes will readily occur to those skilled in the art, it is not desired to limit the invention to the exact construction and operation shown and described. Therefore, all suitable modifications and equivalents fall within the scope of the invention.